IN THE DRAWINGS:

Please replace Figures 7A-7J filed on December 12, 2005 with the attached substitute Figures 7A-7J. Marked-up copies of Figure 7A-7J are also provided to show changes made.

REMARKS

In the Office Action dated August 1, 2008, claims 37, 42-43, 47 and 52-55 are pending in the application, of which claims 37, 42, 43 and 47 are allowed. Claims 52-54 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Claim 55 appears to have been mistakenly omitted from the list of claims rejected. The previous submission of replacement drawings is also objected to because marked-up copies showing changes made to the drawings are not provided as required under 37 C.F.R. §1.121(d)(1), and also because the replacement drawings allegedly contain new matter.

This Response addresses the Examiner's rejection and objections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Replacement Drawing Sheets:

Figure 7 of record contains errors in the numbering of nucleotides and amino acids which Applicants intend to correct.

When the present application was filed as a national phase application under § 371 based on PCT/AU96/00668, Figure 7 consists of eleven (11) sheets and sets forth the alignment of murine and human NR4 sequences. The eleven sheets include a first sheet (i.e., Sheet 13 of 24 or "13/24") showing the manner by which the next ten (10) sheets should be joined with one another to present the full alignment of the sequences; and ten sheets showing the actual alignment of the sequences, which are labelled as Figure 7(i) to Figure 7(x) at the bottom, or 14/24 to 23/24 on the top of the sheets, respectively. Each of the ten sheets of Figures 7(i)-7(x)

also contains dashed lines along two of its borders, which are conventionally used to indicate how the sheet is joined with other sheets.

Replacement drawing sheets for Figure 7 were filed on December 12, 2005, simply to relabel Figures 7(i)-7(x) as Figures 7A-7J, in order to be consistent with the description of the drawings in the specification. There was no change made to the contents of the drawings themselves in this December 12, 2005 submission.

However, Figures 7A-7J contain an error in the numbering of the nucleotides and amino acids for murine NR4. When the murine and human NR4 sequences are aligned to create Figures 7A-7J (i.e., original Figures 7(i)-7(x)), two gaps have been introduced into the murine sequence in order to maximize alignment of the amino acid sequences: one after the amino acid at position 20 and the other one after the amino acid at position 192. See the description of Figure 7 at page 32 of the specification. Clearly, these gaps inserted into the sequence for alignment should not be included when counting the number of nucleotides and amino acids in murine NR4, which does not alter over what is shown in Figure 1 (i.e., the nucleotides and amino acids of NR4) and noted at Example 6. However the gap introduced after the amino acid at position 192 has mistakenly been included in the numbering shown for murine NR4 in Figure 7, being counted as three nucleotides and as one amino acid, with the numbering shown after that gap being displaced by three nucleotides and one amino acid. Therefore, the nucleotide and amino acid numbering for murine NR4 in Figure 7 is correct up to nucleotide 576 and amino acid 192 on Figure 7F. Thereafter, the nucleotide numbering is out by three, and the amino acid numbering is out by one because as noted above the gap introduced after the amino acid at position 192 has been included in the respective counts. The

errors and the corrections are apparent when one compares the murine NR4 sequence numbering of Figure 7 against its numbering as disclosed in Figure 1, or in fact if one simply counts the nucleotides or amino acids.

Accordingly, Applicants re-submit herewith a substitute set of Figure 7 (i.e., Figures 7A-7J) to correct the numbering errors, together with marked-up copies of Figures 7A-7J showing the changes made to the drawings. Applicants respectfully draw the Examiner's attention to the fact that in the replacement drawings submitted herewith, the modifications are made only to the numberings of amino acids and nucleotides, and there is no error and hence no modification needed in the actual alignment of the sequences. Further, although modifications are made only to the numberings that appear in Figures 7E, 7G, and 7I, Applicants have provided herewith an entire substitute set and a marked-up set of Figure 7 (i.e., Figures 7A-7J), such that the Examiner can readily assess the accuracy of the submission.

In view of the foregoing, Applicants respectfully submit that the replacement drawings submitted herewith do not introduce new matter, and fully comply with the provisions of 37 C.F.R. § 1.121(d)(1). Withdrawal of the objection to the drawings is respectfully requested.

35 U.S.C. §112, First Paragraph

Claims 52-54 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that the references made in claims 52-54 to an isolated polypeptide comprising amino acids 28-426 or 28-342 of SEQ ID NO: 4, or comprising an amino acid sequence having at least 95% identity with amino acids 28-426 or 28-342 of SEQ ID NO: 4, represent new matter.

More specifically, while recognizing that Figures 1 and 7 provide alignment of the complete murine and human IL-13 receptor α-chain, the Examiner is of the opinion that these drawings do not allow one to naturally arrive at the polypeptide species composed of the fragment T28-Q426 of SEQ ID NO: 4 or the polypeptide species composed of T28-T342 of SEQ ID NO: 4, let alone a polypeptide having at least 95% identity thereto which binds IL-13.

The Examiner's reasons given for the rejection center around an alleged lack of explicit disclosure of the signal sequence of the human IL-13 receptor α-chain (SEQ ID NO: 4). Specifically, the Examiner states that "the signal sequence for human IL-13 receptor was not known or deduced at the time of filing" of the present application. Page 6, lines 2-4 of the Action. Further, the Examiner states that the signal sequence of the human IL-13 receptor is not the same as the murine IL-13 receptor so a direct comparison cannot be made so as to allow one to 'naturally arrive' at the polypeptide" species recited in the claims. Page 6, lines 4-7 of the Action. Moreover, the Examiner contends that the prior art cannot conclusively predict the signal sequence, or the sequence of the mature or soluble form of the NR4 receptor. Page 6, last paragraph of the Action.

Applicants respectfully disagree. The Examiner has apparently taken an unduly restricted view of the teachings provided in the specification and is practically requiring a literal recitation of the claimed polypeptide species in the specification.

Applicants respectfully submit that the law does not require that the claimed subject matter be described in the specification *ipsis verbis* in order to satisfy the written description requirement. Rather, the relevant inquiry is whether the application has conveyed with *reasonable* clarity to *those skilled in the art* that the inventors had possession of the claimed

invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555m 19 USPQ2d 1111 (Fed. Cir. 1991). Where an element is not explicitly described, it may nevertheless be implicit or inherent in the specification if one of ordinary skill in the art, reading the original disclosure, can reasonably discern the limitation at issue. *Chiron Corp. v. Genentech, Inc.*, 268 F.Supp.2d 1148, 1167 (U.S. E.D. Cal., 2002) (citing *Crown Operations Int'l, Ltd. V. Solutia, Inc.*, 289 F.3d 1367, 1377 (Fed. Cir. 2002)). Further, the Patent Office shall consider expert declaration that explains why those skilled in the art would have understood the application to have adequately described the relevant subject matter. See, e.g., *In re Allen*, 76 F. 3e 1168, 37 U.S.P.Q. 2d 1578 (Fed. Cir. 1996).

Applicants respectfully submit that the application has conveyed with reasonable clarity to those skilled in the art that the inventors had possession of the claimed polypeptide species at the time of filing. In support of this position, Applicants provide herewith a Declaration of Professor Angel Lopez.

Professor Lopez has been working in the area of cytokines and cytokine receptors since 1982, and is well recognized internationally as an expert in this area. Professor Lopez has published his work in reputable and peer-reviewed international journals, with the majority of the 169 publications in the area of cytokines and cytokine receptors.

Professor Lopez testified in the Declaration that those skilled in the art would conclude that an isolated polypeptide comprising amino acids 28-426 or 28-342 of SEQ ID NO: 4 is supported by the present application as originally filed and is part of the present invention. See Paragraph 4 of the Declaration. Professor Lopez stated that his opinion is based

on his review of the specification and drawings, as well as his consideration of the relevant art at the time the present application was first filed in 1996.

Specifically, Professor Lopez observed that prior to the filing of the present application, the family of haemopoietin receptors were well documented in the art and certain features had been recognized as being conserved and characteristic amongst the family; for example, both conserved cysteine residues and a five amino acid motif (WSXWS) in the extracellular domain. See Paragraph 6 of the Declaration. Professor Lopez provided in Exhibit 2 an illustration of the basic structure of haemopoietin receptors, showing that haemopoietin receptors have a single extracellular domain, transmembrane domain and cytoplasmic domain.

Professor Lopez also observed that the present application is based on the identification of a novel haemopoietin receptor, referred to as "NR4" or "IL-13 receptor α-chain". The present application discloses the amino acid and nucleotide sequences of both murine and human NR4. The full-length amino acid sequences for murine and human NR4 are set forth in SEQ ID NO: 2 and SEQ ID NO: 4, respectively. Additionally, Professor Lopez observed that among the various embodiments of the invention, the present application discloses isolated recombinant polypeptides comprising a sequence substantially as set forth in SEQ ID NO: 2 or 4, or part of the IL-13 receptor α-chain, which bind IL-13 and may be in soluble form or expressed on cell surface, as well as pharmaceutical compositions containing an IL-13-binding portion of the receptor for use in modulating immune response and treating, e.g., inflammatory conditions. See Paragraph 5 of the Declaration.

Professor Lopez then discussed more specifically the detailed characterization of the murine NR4 receptor in the present application. See Paragraph 7 of the Declaration. Professor Lopez then concluded:

> "From these disclosures, it would be apparent to one skilled in the art that cleavage of the identified signal sequence would result in a mouse mature protein composed of T27 to P424 of SEQ ID NO: 2, and that this mature form of the protein is that which would normally be expressed on the cell surface. ..... It would also be apparent that amino acids T27-T340 represent the extracellular region of the mouse receptor, which would be readily appreciated by those skilled in the art to constitute a soluble form of the receptor that binds IL-13. Given the entirety of the '568 application, including especially the discussion of soluble and cell surface forms of the receptor, it is clear in my opinion that the '568 application has adequately disclosed the two murine polypeptides, T27 to P424 and T27-T340 of SEQ ID NO: 2 (representing the mature form and extracellular region of the murine receptor, respectively), as embodiments of the invention." Paragraph 8 of the Declaration.

Professor Lopez then explained why those skilled in the art would have understood from the application that the polypeptide composed of T28-Q426 of the human NR4 receptor and the polypeptide composed of T28-T342 of the human NR4 receptor are adequately disclosed. First, Professor Lopez took notice of the fact that at the time the present application was first filed in 1996, there was already a general acceptance in the art that human molecules would be more biologically relevant in humans than the murine counterpart, especially when therapeutic treatments of human patients are contemplated such as in the current application. See Paragraph 9 of the Declaration. Professor Lopez stated that it is apparent that cell surface and soluble forms of human NR4 are also parts of the present invention, given the references to both cell surface and soluble forms of NR4 and the clearly expressed interest in the human forms of NR4. See Paragraph 9 of the Declaration.

Next, Professor Lopez explained that the present application discloses an alignment of the murine and human NR4 sequences, which naturally identifies the signal sequence and transmembrane region of the human NR4 receptor. See Paragraph 10 of the Declaration. Professor Lopez noted that alignment of sequences of known related polypeptides is an alternative approach commonly used in the art for determining the various domains of proteins. See Paragraph 11 of the Declaration. Professor Lopez explained that given the high level of sequence identity and the structural features characteristic of the haemopoietin receptor family, those skilled in the art would have readily obtained the same alignment between the two proteins, as presented in Figure 7 of the present application. Professor Lopez stated:

> "Once two highly homologous amino acid sequences from two different species are aligned, it is straightforward to translate the characterizations made about one of the sequences to the other. In the case of the '568 application, it is immediately apparent from the alignment shown in Figure 7 that amino acids 28-342 of human SEQ ID NO: 4 correspond to the extracellular domain (amino acids 27-340) of the murine receptor; and that amino acids 28-426 of human SEQ ID NO: 4 correspond to the mature form (amino acids 27-424) of the murine receptor." Paragraph 13 of the Declaration.

To conclude, Professor Lopez stated that the present application provides sufficient support for the polypeptides composed of amino acids 28-342 and amino acids 28-426 of SEQ ID NO: 4, respectively, and that those skilled in the art would have naturally arrived at the conclusion that these two polypeptides are parts of the present invention, representing the soluble and cell surface forms of the human receptor, respectively.

Applicants respectfully submit that in view of the specification and drawings as originally filed, and as supported by the Declaration, those skilled in the art would have concluded that the application has conveyed with reasonable clarity to those skilled in the art

that at the time of filing, the inventors had possession of the claimed polypeptide species composed of amino acids 28-342 or 28-426 of SEQ ID NO: 4.

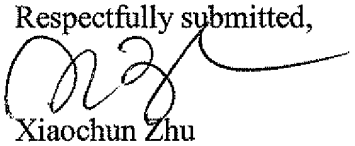
Further, Applicants respectfully submit that the specification also provides clear support for homologous polypeptides, including recombinant polypeptides having at least 95% identity to relevant sequences and polypeptides; see, e.g., page 6, lines 9-29; page 9, lines 1-5 and 18-19. In light of these disclosures, and having established that the specification adequately describes a polypeptide composed of amino acids 28-342 or 28-426 of SEQ ID NO: 4, Applicants submit that the specification has also adequately described a polypeptide having at least 95% identity to a polypeptide composed of amino acids 28-342 or 28-426 of SEQ ID NO: 4.

Accordingly, Applicants respectfully submit that the subject matter of claims 52-55 are fully supported and adequately described in the application as originally filed, and do not introduce new matter. Withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Conclusion

In view of the foregoing amendments and remarks, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Xiaochun Zhu
Registration No. 56,311

Scully, Scott, Murphy & Presser, P. C.
400 Garden City Plaza-STE 300
Garden City, NY 11530
(516) 742-4343 (XZ:ab)
Encs.: Declaration (with Exhibits 1-3); Replacement drawings (Figs. 7A-7J) with marked-up copies.